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Prefrontal oxygenation during executive tasks in children with developmental coordination disorder

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Prefrontal activation during executive tasks in children with developmental coordination disorder: A NIRS study

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ABSTRACT

We examined activation of the prefrontal cortex in children with Developmental Coordination Disorder (DCD) (ages 8 to 12 years) using near-infrared spectroscopy (NIRS). Seven children with DCD and 7 typically developing children were tested for blood oxygenation levels in the prefrontal cortex during completion of the Stroop, Wisconsin Card Sort Tasks and Go/Nogo tasks. The hypothesis that the groups would perform with similar accuracy, but show differential brain activation was supported in the Stroop and Wisconsin Card Sort, but not the Go/No Go task. The typically developing children showed trends toward increased right hemisphere activation during the Stroop and Go/ Nogo tasks and significant right hemisphere activation during the simple reaction time task, while DCD activation exhibited similar activation between hemispheres. This suggests that children with DCD use different neural circuitry to accomplish tasks regardless of the type of processing necessary.

CHAPTER 1 - INTRODUCTION

Developmental coordination disorder (DCD), is a childhood disorder characterized by impaired maturation of gross and fine motor coordination. These children experience problems with visuoperception, spatial integration, balance, sequencing, and coordination (Dewey & Kaplan, 1994; Hoare, 1994; Visser, 2003). According to the Diagnostic and Statistical Manuel IV (DSM-IV), a child with DCD has motor skills that fall well below those expected for his or her chronological age and measured intelligence (DSM-IV, 1994). These limitations must have a negative impact on the child's functional ability to perform activities of daily living and academic achievement.

Since its addition to the DSM-IV, DCD has received significant attention from clinical researchers acknowledging the disparity between its statistical prevalence and the number of children who are actually affected. Six percent of school-aged children are thought to be affected by DCD; this is an indication that a large number of children remain undiagnosed and untreated (Rodger et al., 2003; Visser, 2003).

Because the etiology and prognosis of the disorder are not well understood, diagnosis is problematic. First, the diagnostic criteria for the research are inconsistent. Study inclusion is generally based upon Movement Assessment Battery for Children (M-ABC) performance with the accepted range of scores at or below the 15^{th} percentile (Rodger et al., 2003; Visser, 2003). The various cut-off margins do little to distinguish this population (i.e. anything below the 15^{th} percentile), and it limits the generalizability of the results and fails to contribute to defining the features of DCD. Current trends within the research have established scores below the 5^{th} percentile. This trend is expected to better characterize the population. Moreover, a low score on the MABC is not sufficient to diagnose DCD; a pediatrician must diagnose DCD.

Another reason the etiology and prognosis of DCD have been difficult to establish is that many studies have failed to acknowledge the cognitive aspect of the disorder. Issues with academic achievement, as well as motor coordination identify affected children. Studies have shown that despite average to above average IQ, these children tend to perform significantly below average in school. The combination of motor and cognitive problems suggests some similarities between DCD and other well-explored neurodevelopment disorders, such as attention deficit hyperactivity disorder (ADHD) and autistic disorder (AD).

The relationship between DCD and other disorders implies yet another etiological and prognostic problem. The soft signs of DCD involve motor and cognitive problems in addition to substantial sensory deficits. The visuoperceptual and perceptuo-motor difficulties, as well as, academic achievement issues indeed elucidate the existence of subtypes and comorbidities (Dewey & Kaplan, 1994; Hoare, 1994; Visser, 2003; Wisdom et al., 2007). The lack of heterogeneity in DCD samples clearly poses a problem in defining the disorder and characterizing the ability and deficits of these children. Approximately 50% of children with DCD also have ADHD. Similarly, 50% of children with ADHD also have DCD (Kadesjo & Gilbert, 1998; Pitcher et al., 2003). Despite their distinctiveness, the significant degree of comorbity suggests a shared etiology.

Neuropsychological and physiological evidence on ADHD has contributed substantially to what is known about the neural underpinnings of the condition. Like DCD, ADHD is a neurodevelopment disorder that has been associated with dysfunction in the prefrontal cortex, anterior cingulate cortex, somatosensory areas, parietal cortex and subcortical areas (Aron & Poldrack, 2006; Halperin & Schulz, 2006; Luders et al., 2009; Makris et al., 2009). Typified by inattention, impulsivity and hyperactivity, symptoms of ADHD have been linked to a generalized response inhibition deficit, and overall executive function (EF) abnormalities (Castellanos et al.,

2006; Halperin & Schulz, 2006). Executive functions (EF) are thought to manage novel situations/sequencing with judgment, planning, decision making, working memory, attention maintenance, inhibition and error correction/ management, and research has linked EFs to the functions of the prefrontal cortex (PFC) and the anterior cingulate (ACC) (Castellanos et al., 2006; Pasini et al., 2006).

As shown in neuroimaging research, EFs are likely housed primarily in the PFC and ACC. Near-infrared spectroscopy (NIRS), a brain imaging technique used to determine changes in oxygenated and deoxygenated hemoglobin concentration, has shown differences in prefrontal perfusion between adults and children. Specifically, decreased oxygenation of the prefrontal cortex is notable in children and adolescents when compared to adults performing tasks of executive function (Kawai et al., 2008). This reflects the expected later development of the frontal lobe in humans. Furthermore, decreased oxygenation has been observed in children with ADHD in the left lateral prefrontal area, when compared to age-matched controls (Weber et al., 2005).

Although extensive research has illuminated the psychology and physiology of ADHD, significantly fewer studies have been conducted on DCD. Neuroimaging data and neuropsychological testing have implicated the cerebellum, striatum, white matter tracts (extending from the cerebellum to the anterior parts of the brain), corpus callosum, parietal cortex, ACC, and the PFC in DCD (Querne et al., 2008). Using fMRI, Querne and associates found that despite hypoperfusion noted in the left lateral PFC, children with DCD can perform certain EF tasks at the same level as those age-matched controls. Interestingly, unlike the controls, the children with DCD had greater activation of the ACC, an area associated with error detection and correction (Querne et al., 2008). This unique activation suggests that the ACC may be a part of a distinct circuitry in children DCD that allows them to perform behaviorally in a similar fashion in

spite of decreased activation of brain areas thought to be critical for successful EF task performance. Moreover, loading the PFC with a secondary task may illuminate EF deficits in children with DCD. Presenting a dual task may strain the circuit deficiencies exposing behavioral EF differences. The current study aims to further examine the relationship between executive functions of children with DCD, while recognizing the considerable overlap between DCD and ADHD. To properly characterize the problems, the research must not necessarily strive to exclude the comorbidities, but rather identify the differences between them, and use the differences to distinguish both typical behaviors and effective treatment options. Using neuropsychological testing and NIRS, the executive functions and the prefrontal activity will be assessed in children with DCD, children with DCD and ADHD, and typically-developing children. The participants are eight to twelve year-olds, and those in the DCD groups will be at or below the 9^{th} percentile of motor impairment on the MABC. The typically-developing group (TD) will be above the 25^{th} percentile on the MABC.

It was hypothesized that children with DCD would behaviorally perform the tasks in a manner similar to TD, in the Stroop, WCST and the GNG task, but not the GNG-DT. It was further predicted that the underlying brain activation would be different in all tasks. More specifically, we hypothesized that the TD children would activate the right hemisphere to a greater degree than the left hemisphere, whereas the children with DCD would not show this rightward lateralization.

CHAPTER 2 – REVIEW OF LITERATURE

Few studies have focused on executive processing in children with DCD, or associated brain activity. Further, most of the current research on cognitive processes associated with DCD is directly linked to research on children with ADHD. These studies have revealed substantial connections between cognitive processes and motor impairments, and have identified a large population of children who are impaired on both levels. Convergence of the symptoms of ADHD and DCD suggests they share neural underpinnings. The following review examines the development of executive functions (EFs) and the related neural structures of typically developing children (TD), as well as the current literature on the executive and motor dysfunction of children with ADHD as it relates to DCD.

Executive function is a psychological construct ascribing cognitive processes, such as mental flexibility, working memory, planning, and inhibition to an endogenous supervisory system that is responsible for controlling and directing behavior. Cognitive development has been associated with the maturation of such EFs. Thus, the ability to control thoughts, actions and movement improves with development (Ardila, Pineda, & Rosseli, 2000).

Mental flexibility, or set-shifting, is the ability to adapt behavior in response to changing rules, goals, or environmental circumstances. Conceptually it addresses the ability to shift attentional focus from one point of fixation to another. The maturation of set-shifting is highly correlated with working memory, or the ability to hold and manipulate information in the mind in order to perform complicated tasks. Set-shifting working memory and inhibition have been successfully measured with the Wisconsin Card Sort Task (WCST) (Head, Kennedy, Rodrigue & Raz, 2009; Miyake et al., 2000).

The WCST involves the presentation of a number of stimulus cards that have shapes on them that differ in number, color, and design. The participant is given a set of cards, and told to match each stimulus card according to an unknown rule that must be discovered via feedback. The participant receives feedback about match success. Throughout the test the rules are changed and the time as well as number of errors made to arrive at the new strategy is compiled to generate a score. The test is thus analyzed on two different levels of performance: perseverative errors, or how many errors are made after the rule changed, and failure to maintain set, or failing to maintain the current rule.

Cognitive growth and performance on the WCST occur concomitantly among typically developing children (Cepeda, Kramer & Gonzalez de Sather, 2001; Moriguchi & Hiraki, 2009). The development of set-shifting and working memory, as measured by performance on the WCST, is comparable to young adults by 12 years-of-age on perseverative errors, while failure to maintain set does not reach adult performance levels until age 13 to15 (Ardila, Pineda, & Rosseli, 2000; Bujoreanu & Willis, 2007; Welsh et al., 1991). Bujoreanu and Willis (2007) examined set-shifting using the Wisconsin Card Sort Task (WCST) in six to nineteen year-olds. They found that completed stimulus card categories increases, efficiency increases, and differences in task difficulty emerge as a function of the sorting criterion as children develop. Perseverative errors and failures to maintain set also decrease.

Huisinga, Dolan, and van der Molen (2006) explored the developmental trends of working memory and set-shifting in children aged seven to twenty-one using the WCST. They concluded set-shifting as well as working memory continues to develop into adolescence, and that performance improvement on the WCST reflects continued development of both of those

executive processes. Trajectories for response inhibition and WCST performance also follow this pattern (Nigg, 2000).

Executive functions, such as mental flexibility, planning, working memory, and inhibition have also been shown to be reliably measured by the Tower of Hanoi (TOH) task (Bishop et al., 2001; Bull, Espy, & Senn, 2004). This task requires the participant to arrange a set of disks into a different conformation in the fewest number of moves possible. The disks are of different sizes and only one disk can be moved at a time along three pegs. A larger disk cannot be stacked on top of a smaller disk. Bull, Espy, and Senn (2004) tested set-shifting in 118 children with a mean age of four years using the TOH. Matching for age, sex and vocabulary level, they found that performance was related to age, but not sex or vocabulary level. They concluded that better performance was associated with greater ability to set shift. Bishop et al. (2001) concurred using an older group of children. Combining the research, age and performance on the TOH are clearly related to multiple executive processes.

Response inhibition is an executive function that involves attention and the ability to overcome the tendency toward prepotent responses. In other words, executive control guides goal-oriented behaviors and schedule actions to minimize conflict when overcoming habitual responses. The first prominent maturational milestone of attention occurs between five and seven years of age (known as the 5-to-7 shift), while peaks in response inhibition occur between eight and twelve years-of-age (Bartgis et al., 2008). Go/ Nogo (GNG) tasks have been shown to be reliable measures of both attention and inhibition.

Bartgis et al. (2008) used an auditory GNG task to assess attention and response inhibition. The researchers presented stimuli to both ears simultaneously using soft non-target tones, and loud target tones. There were four phases of tone presentation; the first two contained target tones

(normal volume) and silent blanks (no sound) and the second two contained target tones and non-target tones (very low volume). Phases two and four included a distracter, which were segments from a popular children's movie. The researchers concluded that while both attention and response inhibition are involved in the 5-to-7 shift of normal children, seven-year-olds performed tasks involving distraction better than five-year-olds.

The most significant factor in the distracter phases was age, while response inhibition measured similarly between both age groups. This supports the notion that an attentional shift takes place between age five and seven, and developments in response inhibition have not yet reached measurable differences within this age range. In typically developing children, the maturation of attention precedes that of response inhibition, such that differences in attention can be observed between five and seven years, while differences in response inhibition are observed around eight or nine years of age, reaching adult-like levels by the age of twelve (Bartgis et al., 2008; Durston et al., 2002; Spronk, Jonkman, & Kemner, 2008; Van den Wildenberg & Van der Molen, 2004).

Tillman et al. (2008) used a GNG paradigm in a study aimed at relating the developmental trajectories of attention and inhibition in typically developing children to ADHD- related behaviors by comparing the visual stop-signal reaction time (SSRT) and probability of inhibition. Behaviors associated with ADHD were assessed using the Connor's scale for teachers. The children were instructed to press a key repeatedly when a green car drove onto a screen. If there was a red stop sign in front of the green car, the children were instructed not to press the key.

Motor response inhibition was shown to improve significantly with age in children between four and twelve years old. Stop signal reaction time scores showed the greatest change in the five to six and six to eight age-groups. Longer SSRTs (i.e. poorer inhibition capacity) were associated

with higher ratings of inattention, while more inhibition errors were linked to higher ratings of hyperactivity and impulsivity. Tillman et al. concluded that the presence of behaviors associated with ADHD moderates responses that require inhibition and working memory.

The development of attention was evident in five and six year-olds, whereas inhibition became apparent in children between six and nine years-of-age. Moreover, reaction times were related to attention-related behaviors, while errors were related to impulsivity and hyperactivity. These data match the maturational peaks of the frontal lobe documented to occur during the same developmental time frame (Thatcher, 1991).

Consistent with the data on typically developing children, Spronk, Jonkman and Kemner (2008) described response inhibition, but not attention is still immature at seven years-of-age in children both with and without ADHD. Children between five and seven years old performed a GNG task, where one of eleven letters was presented on a monitor. The children were instructed to press a button with the right hand when the letter "X" was presented, but only if was preceded by the letter "A" (A-X sequence; the Go condition). When "A" was followed by any other letter, the children were instructed not to press the button (A-not-X sequence; the Nogo condition). Event related potentials (ERPs) were simultaneously taken and related to GNG performance on both cued (A-X and A-not-X) and non-cued tasks (all other letters, not "A" or "X"). The ERP components were assessed with respect to response preparation, inhibition, and conflict monitoring processes in order to examine the brain activity underlying executive functions and attention deficits.

Attention deficits were observed in children with ADHD between five and seven years, making significantly more Go errors than matched controls. Go reaction time and variability did not differ between groups. The researchers concluded that the general immaturity of the frontal lobes resulted in high response variability in both groups because the frontal cortex has been

shown to contribute significantly to the maintenance of attention, as well as performance variability. In line with the research of Bartgis et al. (2008), there appears to be a significant developmental shift of attention between five and seven years-of-age.

The ADHD and TD groups demonstrated a strong effect in conflict monitoring, but not response inhibition. On the GNG task, ERP data indicated activity in the fronto-central and parietal networks. Because ERP activity and task performance were comparable between the groups, the data support that the fronto-parietal circuitry needed for successful conflict monitoring is a developmental phenomenon that not observed until at least seven years of age. Further, the marginal effect and absence of between-group differences observed in response inhibition indicates that the function remains immature in children seven years and younger.

Supporting these conclusions, previous research indicates that TD children between eight and twelve years develop conflict monitoring prior to inhibition, an indicator of the maturation of normal response inhibition (Johnstone et al., 2007). Decreased ERP activity in the fronto-central locus (conflict monitoring) has been associated with ADHD children between seven and fourteen years of age, when compared to controls (Brandeis et al., 2002).

The research shows that attentive and conflict monitoring processes precede response inhibition, and that development begins at about six years of age (i.e. attention and conflict monitoring). Inhibition is fully apparent by about age nine. For purposes of investigating executive dysfunction, assessing performance on the behavioral tasks and corresponding brain activity can reveal attentional deficits in 5 to 7 year-olds and inhibitory deficits in 8 to12 year-olds.

Taken together, the executive processes follow developmental trajectories that complement maturational shifts in the prefrontal cortex. Developments in set-shifting, planning and, working memory begin as early as three years of age and reaches adult levels by the age of 15. Response

inhibition is the result of the development of attention and conflict monitoring, where the development of attention precedes that of conflict monitoring. Peaks in attention and conflict monitoring are observed between five and six years and seven years, respectively, whereas response inhibition does not begin to develop until at least seven years, and does not reach adult levels until at least twelve years.

Developmental peaks in performance on executive tasks have been shown to occur in parallel with drastic maturational changes in the prefrontal cortex during childhood and adolescence (Durston et al., 2002; Dumontheil, Burgess, & Blakemore, 2008; Funahashi, 2001; Giedd, Blumenthal, & Jeffries, 1999; Tsujimoto, 2008; Welsh et al., 1991). The developmental trajectories of executive functions match the maturation peaks documented to occur within the frontal lobe (Miyake et al. 2001; Thatcher, 1991). Furthermore, neuroimaging studies show that the volume of the white matter increases along with a reduction in the density of neurons and their synapses. Improved behavioral performance is evidence that distributed neural networks associated with the development of complex cognitive processing are established. Magnetic resonance imaging confirms that grey matter volumes peak during adolescence. Thus, the volume of the prefrontal cortex increases into adolescence, and is then followed by a pruning process that continues into early adulthood. These anatomical changes are consistent with increases in cognitive speed and efficiency (Giedd et al., 1999).

Moriguchi and Hiraki (2009) documented the neural development of cognitive shifting in three and five year olds using NIRS. They demonstrated that the inferior prefrontal cortex is activated during shifting tasks in both age groups, despite the significant differences in perseveration. Three year-olds perseverate more than five year-olds. The researchers concluded that the neural origins of shifting are housed in the prefrontal cortex, a conclusion consistent with

the abundance of research suggesting that executive functions (i.e. set-shifting) are derived from the prefrontal cortex (Ardila et al., 2000; Booth et al., 2003; Brandeis et al., 2002; Casey et al., 1997; Dumontheil, Burgess, & Blakemore, 2008; Durston et al., 2002; Moriguchi & Hiraki, 2009; Oner et al., 2005). This suggests that the shifting associated with the WCST is related to the inferior prefrontal cortex and differences can be observed with NIRS.

The TOH has not been linked to the maturation of any specific underlying neurological mechanisms (Bishop et al., 2001). The performance improvements on the TOH have been shown to co-occur with the known staging of frontal lobe development (Thatcher, 1991), suggesting that processes necessary for TOH performance are somehow linked to the frontal lobe, but that the specific parameters of that physiology have not yet been established. Moreover, consistent with the notion that the TOH is a measure of planning, set-shifting, working memory and inhibition, people with prefrontal lesions have been shown to perform poorly on the TOH, as well as the TOL (Hernandez et al., 2002; Kopecky et al., 2005).

Other neurological imaging studies examining the role of the rostral prefrontal cortex in inhibition has been somewhat equivocal. Most indicate decreases in regional blood flow in adults compared to adolescents. Durston and colleagues (2002) did not find these differences, using a go/no go task. Notwithstanding, Casey et al. (1997) and Booth et al. (2003) did observe such findings, where performance of a GNG task resulted in decreases in left prefrontal perfusion in normal children and no decreases in adults. The latter studies support the notion that EFs are housed in the prefrontal area and that blood perfusion changes as a function of cognitive development. Furthermore, Rubia et al. (2003) reported increased right hemisphere activation during the stop task (an inhibition task) in healthy young adults. This implies that higher level

cognitive processing may be utilizing the right prefrontal lobe more than the left and that damage to that area may be particularly problematic for EFs.

Prefrontal dysfunction is associated with poor executive performance. Deficits in judgment, planning inhibition, mental flexibility and working memory characterize the dysfunction (Moriguchi & Hiraki, 2009). Attention deficit/hyperactivity disorder is known to primarily affect EFs, and has been related to abnormal prefrontal function (Negoro et al, 2010; Weber, Luetschg, & Fahnenstich, 2005). In addition to cognitive problems, ADHD is also associated with motor impairments (Piek, Pitcher & Hay, 2003). The variably diminished motor dysfunction provides the segway to the possible relationship that exists between ADHD and DCD. Not only is ADHD comorbid in almost half of the cases of DCD, but research indicates that DCD is correlated with impaired executive processes (Kadesjo & Gillberg, 1999; Pitcher, Piek, & Hay, 2003). The rate of comorbidity and the problematic-definition of the disorder necessitate the subtype characterization that may exist within a sample.

Comparing the EF of children with inattentive and combined-type ADHD with normal children using the TOH, Kopecky et al. (2005) showed that the combined group had the poorest performance. Other studies have concurred (Nigg et al., 2002) implying that the combined type disorder has the greatest EF deficits. Differences in executive ability profiles between the purely cognitive subtypes and the cognitive/ motor subtypes substantiate the idea that characterizing ADHD, as well as other motor disorders, such as DCD, necessitates subtype differentiation.

In a study examining the relationship between working memory, inhibition, and performance on the WCST within the ADHD population, researchers found that children with ADHD made the same number of perseverative errors as TDs when co-varied for age and IQ (Mullane & Corkum, 2007). However, children with ADHD did fail to maintain set more

frequently. Furthermore, working memory was correlated significantly with perseverative errors, but again, mediated by age and IQ. Although this type of assessment must be cautiously interpreted when identifying children with ADHD, it is a valid and discerning test of executive function within a population of children with ADHD (subtype identification).

High levels of comorbidity between ADHD and DCD suggest similar neurological underpinnings (Kadesjo & Gillberg, 1998; Kadesjo & Gillberg, 1999; Piek et al., 2007; Pitcher, Piek, & Hay, 2003). Piek et al. (2007) assessed four groups of children between the age of six and fourteen years on working memory, set-shifting, and processing speed using the goal neglect task trail making/updating task and a visual inspection task. The different groups were controls, ADHD- inattentive, ADHD-combined and DCD (5^{th} percentile on the MABC). The goal neglect task measures a child's ability to generate and react to goal-directed plans. After learning a specific task, the participants must then ignore it, in order to perform an alternative task. The trail making/updating task involves a target set of letters is presented (A, B, C and D) with the actual target being the order of presentation. The participant must determine whether the letter is within the target set and if it is the current target. It assesses behavioral inhibition and working memory. The visual inspection task is designed to evaluate the amount of time it takes for an individual to discriminate between two different line lengths.

The DCD group had the most errors on the GNT, the most variability, and the longest time on the TMUT, and the longest time on the VIT. These results are consistent with known motor processing deficits associated with DCD. Unremarkable EF measures of the ADHD groups led researchers to conclude that unidentified DCD comorbidities may have played a role (Piek et al., 2007). Wisdom et al. (2007) examined response inhibition in children with DCD and ADHD using the no/no go, TMUT and GNT. They also found no significant differences. Recognizing comorbid

conditions within DCD groups will improve classification and better delineate cognitive functional differences, as well as, associated neural underpinnings.

Pitcher, Piek, and Hay (2003) investigated motor ability within the three subtypes of ADHD. They found that that the children who had the poorest performance on the Purdue Pegboard also scored in the lower 15th percentile on the MABC. Nevertheless, the comorbidity of ADHD and DCD, could not link fine motor deficits to attention deficits.

Similarly, Piek et al. (2004) found little overlap between motor coordination deficits and inattention. They examined the relationship in a sample of 238 children ages seven to fifteen years, assessing reaction time, response inhibition, working memory, and planning. Finding no differences in executive function, the researchers concluded that motor ability accounted for most of the variance in speed-related performance, while inattention was related to performance variability. Moreover, a relationship between motor dysfunction and response inhibition was not supported.

In contrast, the findings from the research of Wilson and Maruff (1999) maintain that there is a connection between motor deficits and inattention. They examined visuospatial attention in children with DCD and in controls. They used a spatial precue task in which a target event, an illumination, occurred in one of two peripherally located areas, the right or left side of the central fixation point. The precue related to the possible location of the target event, preceding the event by 150 ms or 850 ms with 83% accuracy. Participants pressed a keyboard button when the stimulus was detected, and the time from illumination to detection was measured.

The researchers compared the reaction times of valid precues to invalid precues. Valid precues are thought to automatically draw attention to the cued target location, while invalid precues that require the participant to disengage the attention from one location to search for the

target stimulus. Thus, the attention is oriented either automatically or volitionally, and that allocation is controlled with the two different types of cues. The speed with which the participant disengaged attention from the location of the invalid cue, or intentionally re-oriented was measured and used to assess the presence of selective visuospatial deficits. The DCD group demonstrated this deficit when attention required volitional re-orientation, suggesting a relationship between motor coordination problems and specific attention-related difficulties.

Mandich, Buckolz and Polatajko (2002) assessed children with and without DCD between seven and twelve using compatibility tasks to assess deficits in attention as they relate to problematic response inhibition. The researchers found that both groups inhibited unwanted responses with similar reaction times but the DCD group committed significantly more errors. Moreover, the DCD group showed decreased ability to inhibit prepotent responses. Consistent with Wilson and Maruff (1999), DCD groups were characterized by poor response inhibition. Results from the studies on motor deficits and executive function may have differed as a result of different methods of sample characterization, as well as, different attention and inhibition assessment methods.

Another way to investigate a possible relationship between motor abilities and EFs is to examine the development of associated brain structures. Near-infrared spectroscopy (NIRS) is a non-invasive, safe, and practical method for assessing brain function of children, particularly those with ADHD and/or DCD, while performing tasks that measure executive processing. Near infrared spectroscopy measures tissue absorbance of light at the wavelengths of 700-1000 nm. It is used to study changes in hemodynamics and changes in oxygen concentration by measuring the absorbance of various near-infrared wavelengths of oxygenated and deoxygenated hemoglobin. Although NIRS can only measure relative changes, studies have shown it is a sensitive tool for

assessing prefrontal hemodynamic changes. Moreover, the measurements obtained from this tool can be associated with changes in functional activation of the corresponding brain region being evaluated (Herrmann et al., 2006; Irani et al., 2007; Kawai et al., 2008; Negoro, et al., 2010; Weber, Luetschg, &Fahnenstich, 2005).

In a recent study, children with DCD and age-matched controls between eight and twelve years old performed a trail tracing task during PET scanning. Children with DCD displayed differential brain activation from TDs despite similar performance on the behavioral task. Specifically, the DCD group showed less activation in the left parietal and left frontal activation – areas associated with spatial processing and error processing. The data suggest that the DCD group use a different strategy to accomplish a task that utilizes visuospatial processing (Zwicker, Missiuna, Harris, & Boyd, 2010).

Herrmann et al. (2006) used NIRS to assess changes in cerebral oxygenation of the prefrontal cortex as a function of age and gender. Young men and women (mean age 23.8 years) were compared to older men and women (mean age 62.7 years) on a verbal fluency task. The results showed that left and right dorsolateral prefrontal cortex were activated with significant left hemisphere dominance in both groups. That is, the left hemisphere showed a greater concentration of oxygenated hemoglobin and a corresponding decrease in deoxygenated hemoglobin. Bernal and Altman (2009) reported similar left lateralization during the Stroop task, but right lateralization during a GNG motor inhibition task.

Weber et al. (2005) showed an imbalance in oxygenated and deoxygenated blood flow in the left PFC using NIRS during both the short and the extended attention tasks demanded by the trail making test in boys (mean age 10.4 years) with ADHD. Children with ADHD showed significant increases in oxygenated hemoglobin, while controls revealed no changes during the

short attention task. In the extended condition, both groups revealed oxygenated hemoglobin increases, but the control group also showed an increased in deoxygenated blood flow in the left prefrontal area. Overall, the ADHD group had a significantly higher tissue oxygenation index mainly on the left side. The researchers concluded that decreased prefrontal activity was related to poorer performance on the trail-making task within the ADHD group. Furthermore, the impaired performance indicates deficits in EF, illustrating the role of the prefrontal cortex in its mediation.

Hashimoto, Urama, and Abo (2008) investigated hemodynamic changes in the PFC using the WCST. Twenty people with traumatic brain injury (TBI) showed lower total hemoglobin volume in the right PFC during the WCST when compared to non-brain injured people. Although it appears that this evidence is equivocal, it could be indicative of differential hemodynamic changes that occur as a result of different types of neural damage. Many studies have indicated decreased oxygenated blood volume, or activity, in the left prefrontal cortex in neurodevelopmental disorders such as ADHD and autistic disorders, where executive processes are known to be deficient (Brandeis et al., 2002; Hernandez et al., 2002; Irani et al., 2007; Oner et al., 2005; Shaw et al., 2007). This study, however, examined TBI, where upon MRI and CT identified no obvious injury in the prefrontal cortex. The researchers suggested that the differences observed could be related to axonal damage. That is, problematic white matter connections may play a role in the etiology of the executive deficits.

Neurological and neuropsychological data indicate that a relationship exists between motor abilities and executive functions, though the exact nature of lateralization still needs clarification. Further, the significant comorbidity that is associated with DCD and ADHD engender the likelihood of similar neural bases. The current study aims to utilize the information available on

subtyping, tests of executive processing, and NIRS to provide more depth to the understanding of the executive processing of children with DCD.

ABSTRACT

We examined activation of the prefrontal cortex in children with Developmental Coordination Disorder (DCD) (ages 8 to 12 years) using near-infrared spectroscopy (NIRS). Seven children with DCD and 7 typically developing children were tested for blood oxygenation levels in the prefrontal cortex during completion of the Stroop, Wisconsin Card Sort Tasks and Go/Nogo tasks. The hypothesis that the groups would perform with similar accuracy, but show differential brain activation was supported in the Stroop and Wisconsin Card Sort, but not the Go/No Go task. The typically developing children showed trends toward increased right hemisphere activation during the Stroop and Go/ Nogo tasks and significant right hemisphere activation during the simple reaction time task, while DCD activation exhibited similar activation between hemispheres. This suggests that children with DCD use different neural circuitry to accomplish tasks regardless of the type of processing necessary.

CHAPTER 3: Prefrontal oxygenation during executive tasks in children with developmental coordination disorder

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INTRODUCTION

Developmental coordination disorder (DCD) is a childhood disorder characterized by impaired gross and fine motor coordination. These children experience problems with visuoperception, spatial integration, balance, sequencing, and coordination (Dewey & Kaplan, 1994; Hoare, 1994; Visser, 2003). According to the DSM-IV TR, a child with DCD has motor skills below those expected for his or her chronological age and measured intelligence. These limitations have a negative impact on the child's functional ability to perform activities of daily living and academic achievement (American Psychiatric Association, 2000).

Despite average to above average IQ, these children perform below average in school (Dewey, Kaplan, Crawford, & Wilson, 2002). One contributing factor may be impaired executive functioning. Executive functioning (EF) is a set of cognitive processes necessary to conduct goal-directed behaviors, such as those required in novel situations that involve judgment, planning, set-shifting, decision making, working memory, attention maintenance, inhibition, and error correction. These processes have been shown to be mediated in large part by the prefrontal cortex and the anterior cingulate (Castellanos, Sonuga-Barke, Milham, & Tannock, 2006; Pasini et al., 2006; Olson & Luciana, 2008).

Research on the executive functions in children with DCD has produced equivocal results (Mandich, Buckolz, & Polatajko, 2002; Mandich, Buckolz, & Polatajko, 2003; Querne, et al.,

2008; Wilson, Maruff, & McKenzie, 1997). They exhibited impaired EF performance on tasks that require inhibition of incorrect responses and inhibition of responding to distractions (Mandich, Buckolz, & Polatajko, 2002; Mandich, Buckolz, & Polatajko, 2003; Wilson, Maruff, & McKenzie, 1997; Wilson & Maruff, 1999; for review Visser, 2003). Mandich and colleagues (2002) found that children with DCD were more likely to fail to inhibit incorrect manual responses in tasks involving an external event. They administered a task to 7-12 year-olds in which response decisions were made according to the luminance of a cue. The spatial location of the illuminated cue provokes a response to that location before the color analysis is complete (urging a response that leads to a failure to inhibit). The failure to inhibit incorrect manual responses implies that when tasks involve an external event (luminance change) they are less successful at inhibiting response tendencies than typically developing children. Wilson, Maruff and McKenzie (1997) reported similar findings using an attention task in which the eyes were to remain fixated at a location and resist the urge to shift attention to another cued location.

Mandich and associates (2003) also found that children with DCD showed deficits in disengagement and initiation inhibition. Children performed an informative and an uninformative spatial precue task. They responded to target locations with a corresponding button press to green precue arrows, but not to target locations of red circles (catch trials). During the informative condition (participants knew the likelihood of the cue indicating the target was high), the precue arrow indicated a target location in about 80% of trials (52 valid, 12 invalid, 16 catch trials) and during the uninformative condition (did not know about the likelihood of the cue indicating the target), the precue was only valid in about 25% of the trials. In the informative condition, children with DCD took longer to disengage from the cued location demonstrating a deficit in disengagement inhibition. However, in the uninformative condition,

attention automatically followed the direction of the arrow indicating that children with DCD have an initiation inhibition deficit (poor inhibition of the urge to move attention). They showed a similar difficulty with inhibiting prepotent responses during catch trials. Wilson and Maruff (1999) obtained comparable results in a study using a spatial orienting task that involved fixation of attention at a specified location and response to a peripheral cue. Children with DCD had difficulty disengaging attention and inhibiting incorrect responses (Wilson & Maruff, 1999).

Inhibition is a foundational executive function; however most tasks used to assess it are not pure measures (e.g. Miyake et al., 2000) tapping into multiple inhibitory processes (Nigg, 2000). Garon et al. (2008) made a distinction between inhibition tasks that involve working memory (complex response inhibition) and those that do not (simple response inhibition). Complex response inhibition involves some kind of rule that must be held in mind or necessitates the inhibition of one response and the production of another. Nigg (2000) further differentiates the neurological and behavioral processes associated with cognitive, behavioral and emotional inhibition. Bernal and Altman (2009) reported results that support this notion. Using fMRI during performance of a Stroop task and a GNG motor inhibition task, young adult participants exhibited left lateralized and right lateralized activation, respectively. The authors concluded that the cognitive aspect of the Stroop task and the motor aspect of the inhibition task activate the prefrontal hemispheres differentially. Given that networks that subserve these different types of inhibition are not the same (Alexander, Crutcher, & DeLong, 1991; Bernal and Altman 2009) and the tasks are generally impure (Miyake et al. 2000), discriminating the type of inhibition(s) being utilized may allude to a methodological explanation for equivocal results found in studies on children with DCD and executive functioning.

Contrasting the work carried out by Mandich et al. (2002; 2003) in which EF were showed to be impaired in children with DCD, Querne and associates (2008) did not find differences in successful inhibition. They used a Go/Nogo (GNG) paradigm in children ages 8 to 13. The task required children to press a response key to any letter (go trial) except X (nogo trial). Children with DCD correctly inhibited Nogo trials in a manner similar to their typically developing (TD) counterparts (albeit slower and with more variability).

The different methodologies used by Mandich et al. (2002; 2003) and Querne et al. (2008) may exploit inhibitory networks differentially. The visual spatial attention tasks used by Mandich et al. (2002; 2003) are more difficult and classified as complex inhibitory tasks, as defined by Garon et al. (2000), and the GNG paradigm decribed in the Querne et al. (2008) study is classified as a simple inhibition task. Differences in results derived from the previously described tasks may be attributed to differences in complexity, particularly in consideration of the known visuoperceptual and visuospatial processing problems in DCD which may have further complicated the Mandich et al. studies. Moreover, manipulating the complexity of GNG paradigm to include a dual task would classify it as a complex inhibitory task. Based on this rationale, the increased complexity of the task may elucidate differences in this paradigm that were not observed in Querne et al. (2008)

Although Querne et al. (2008) did not find behavioral differences; they did find differential brain activation during the GNG. Based on fMRI, the TD children showed greater activity in the right hemisphere, whereas children with DCD exhibited greater activity in the left hemisphere. In addition, those with DCD had greater activation of the anterior cingulate, an area associated with error detection, correction and interference control (Posner & Raichle, 1994).

Few studies have focused on EF and their associated brain activity in children with DCD. Neuroimaging and neuropsychological testing have implicated the prefrontal cortex and anterior cingulate in the sequelae of DCD as well as the cerebellum, striatum, white matter tracts (extending from the cerebellum to the anterior parts of the brain), corpus callosum, and parietal cortex (Querne et al., 2008; Zwicker, Missiuna, & Boyd, 2009). Supporting the notion that children with DCD utilize different networks than typically developing children to accomplish the same tasks, Zwicker, Missiuna, Harris and Boyd (2011) showed underactivation in the right middle frontal gyrus and right frontal regions as well as the bilateral parietal lobes and the bilateral cerebellum in children with DCD using fMRI during a trail tracing task. Moreover, less activation in the right frontal gyrus was associated with fewer traces completed in the task. This unique activation during executive tasks suggests that children with DCD may be using a different strategy for problem solving. Thus, there is both behavioral and neural evidence to associate DCD with impaired EF.

Near-infrared spectroscopy (NIRS) is a technique used to assess changes in oxygenated and deoxygenated hemoglobin concentration. This technique has been used to examine differences in brain activation during attentional tasks between children with attention-deficit hyperactivity disorder (ADHD) and TD children (Weber, Luetschg, & Fahnenstich, 2005). Moriguchi and Hiraki (2009) found changes in prefrontal blood oxygenation using NIRS in preschool-aged children while performing the Wisconsin Card Sorting Task (WCST). More specifically, they demonstrated that the inferior prefrontal cortex is activated during the task in addition to showing that the three year-olds perseverated more than five year-olds. The researchers concluded that the neural origins of the EFs necessary to complete this task are housed in the prefrontal cortex, a conclusion that is consistent with the abundance of research (Ardila, Pineda, & Rosseli, 2000; Booth, Burman &

Meyer, 2003; Brandeis et al., 2002; Casey et al., 1997; Dumontheil, Burgess, & Blakemore, 2008; Durston et al., 2002; Moriguchi & Hiraki, 2009).

The purpose of this study was to examine EF in children with DCD compared to TD children using NIRS. Based on the research of Querne and colleagues (2008), it was hypothesized that children with DCD would behaviorally perform the tasks in a manner similar to TD, in the Stroop, WCST and the GNG task, but not the GNG-DT (Go Nogo-dual task). It was further predicted that the underlying brain activation would be different in all tasks. More specifically, we hypothesized that the TD children would activate the right hemisphere to a greater degree than the left hemisphere, whereas the children with DCD would not show this rightward lateralization.

METHODS

Participants

Children between the ages of 8 and 12 were recruited from the local community via flyers and word-of-mouth. Forty-eight children were screened using the Movement Assessment Battery for Children-2 (MABC-2), the Kaufman Brief Intelligence Test (K-BIT2) and the Connor's Parent Scales for ADHD, and Edinburgh Revised Handedness Questionnaire. Exclusionary criteria included: parental report of children with a history of developmental disability, mental disability, neurological disorders, or brain trauma; an IQ less than 90 based on the K-BIT2; and children with a clinical diagnosis for ADHD or a score above the 76^{th} percentile for inattention or hyperactivity on the Connor's Parent Scales. Of the original 48 children, 3 tested below 90 on the KBIT-2 IQ test, 2 were diagnosed with neural conditions after they were entered into the study, 16 children were excluded due to ADHD, 7 were excluded due to problems with equipment, and 1 did not return for the second session.

The DCD experimental group was identified in the following manner: children who scored at or below the 9th percentile on the MABC-2 and who demonstrated functional movement difficulties that markedly impaired their performance of activities of daily living and/or academic performance as evidenced by the MABC-2 questionnaire for parents. Seven children met these criteria, 3 girls and 4 boys. The TD sample was group matched with the DCD sample for age, IQ, and handedness (there was one left-handed child in each group), and performed at the 25th percentile or above on the MABC-2. After matching for handedness, this resulted in a sample of 7 children in the TD group, (2 girls and 5 boys). There were a total of 7 age-matched children in each group (See Table 1 for demographics for each group).

Table 1. Demographics and baseline assessments. Standard deviations are presented in parentheses and the range of scores in brackets.

Group	**DCD**	**TD**	***P***
Age (months)	119.3 (18.1) [97-140]	117.1 (12.8) [96-136]	1.00
MABC-2[1] (percentile)	7.3 (2.1) [5-9]	58.7(26.3) [25-95]	0.0002
MABC-2 Questionnaire	2.4 (0.8) [1-3]	1.3 (0.5) [1-2]	0.007
Beery-Buktenika[2] (percentile)	21.9 (15.8) [6-42]	54.9 (32.7) [12-88]	.0446
K-BIT (IQ)	116 (12.4) [93-132]	118.9 (8.5) [107-131]	0.624

[1]Movement Assessment Battery for Children- 2nd edition
[2]Beery-Buktenika score is a measure of visual-motor integration

All procedures were reviewed and approved by the institutional review board of the university. All participants and parents of participants signed an informed consent prior to the start of the study.

Tests of Executive Function

Stroop. The Stroop task (MacLeod, 1991) was developed to assess response inhibition and speed of response. The traditional color-word task requires the participant to say the color of word rather than read the word. There are congruent trials in which the word is the same as the color in which the word is written (the word "red" presented in red ink) and incongruent trials in which the word and color are not the same (the word "red" presented in blue ink). Naming the color of the word has been shown to take longer and is more prone to errors if they are incongruent.

A numerical form of the Stroop was used in the current study because reading was less automated. So, for example, if the numeral 1 appeared once or the numeral 4 appeared four times, that was considered a congruent trial. Alternatively, if, for example, the numeral 4 appeared once, that was considered an incongruent trial. The child was to respond to the number of times the numeral appeared, not the numeral itself.

Children performed a familiarization task on the computer to associate keys on the keyboard with the numbers one through four using the four fingers on one hand (whichever hand they preferred to use). Once they could associate each number with the correct key, they completed 15 trials of practice in which they were presented with both congruent and incongruent trials. They were instructed to identify the number of numerals they saw on the screen (e.g. press 4 if "1111" appeared). If the trial was performed correctly the word "correct" appeared on the screen. If the trial was performed incorrectly, the word "incorrect" appeared on the screen. Once it was clear the child understood the task, 48 trials of the Stroop-number task were performed without feedback about accuracy (24 congruent and 24 incongruent trials presented in a pseudo-random manner. Reaction time (time from presentation of stimulus to key press) and accuracy of response were measured for congruent trials and for incongruent trials.

Wisconsin Card Sort Task (WCST-64; a short form). The short form of the WCST (WCST-64; Kongs, Thompson, Iverson, & Heaton, 2000) was also used to assess inhibition. As a widely used neuropsychological measure of executive function, it has been shown to be associated with activity in the prefrontal cortex (Moriguchi & Hiraki, 2009). The measure has been validated for people ages 6 to 89. The WCST involves the presentation of 64 stimulus cards differing in number, color, and shape on a computer screen. The participant was told to match each stimulus card according to the number, color, or shape on the card. The rule for the correct match is unknown and must be discovered via feedback from the computer (the word "RIGHT" or "WRONG" written across the screen after each match is made). Throughout the test the rules are changed and the number of errors made in attaining the new rule is compiled to generate a score. Perseverative errors (how many errors made after the rule changed) were measured.

Go/No Go. The Go/Nogo and the Go/Nogo-dual task (GNG-DT) were developed to assess response inhibition and speed of response. They have been shown to be associated with activity in the prefrontal cortex (Miyake et al., 2000). The participants are seated in front of a reaction time board so they could easily reach each of the lights in front of them. Using their dominant hand, they pressed the home button and, when one of the lights was illuminated (after a variable warning tone, from 800ms to 2000 ms), they were to respond as quickly as possible. In addition, simple reaction time was measured in order to provide an index of performance in which prefrontal activity was minimized.

For the simple reaction time task (SRT), only the light at the right center was visible and illuminated during the trial (all other lights were covered). Following ten trials of practice with the SRT, there were a total of 16 trials. For the GNG and GNG-DT, the right and left center lights were visible. When the right light illuminated, the participants had to move as quickly as possible

(which is identical to the SRT test). However, when the left light illuminated, the participants were to stay on the home button, and for the dual task. The participants performed a verbal task Sentences, such as “The dog is brown” and “The boy stands up,” were read to the participants and the participants repeated them immediately. Ten verbal trials were practiced without the movement aspect of the task. During the practice, it was emphasized that pauses between sentences would result in a repeated trial and that simultaneous response to the green light and the verbal task needed to occur. If the participant was not engaged in the verbal task when the light went on (i.e. not listening or repeating), the trial was redone. There were a total of 28 trials with 16 “go” trials and 12 “no go” (inhibition) trials.

Timing of the lights and measurement of reaction time were controlled by a computer interfaced to the reaction time board and appropriate software. Reaction time was measured as time from the “go” signal until the hand moved of the home button until pressing the illuminated button.

Measurement of Prefrontal Blood Flow

Near Infrared Spectroscopy. Near infrared spectroscopy (NIRS) (Oxiplex TS, ISS, Champaign, IL) was used to assess oxygenation in the prefrontal cortex. It is a non-invasive measure of oxy- and deoxygenated-hemoglobin levels in real time with sensors that are secured to the forehead (e.g. Matsui, Tanaka, Yonezawa, & Kurachi, 2007; Moriguchi & Hiraki, 2009). Sixteen emitter fibers deliver photons of light (8 per channel; 4 at the 692 nm and 4 at the 834 nm wavelength) from the oximeter through four emitters that are spaced 1.5 to 5.0 cm apart on each side of the forehead. After the photons are transmitted into the tissue, some of them are absorbed by the tissue. Due to scattering, other photons travel along arc pathways in tissue from the emitter

to the detector fiber-optic bundle penetrating derma, skull, dura, cerebrospinal fluid and prefrontal cortical layers beneath the sensor on the forehead.

Procedures

Children were tested in two sessions; the duration of the first session was approximately 90 minutes and approximately 60 minutes for the second session. In the first session the MABC, 2nd edition, the Kaufman Brief Intelligence Test, 2nd edition and the Beery-Buktenika Test were administered. Relevant medical history and a MABC questionnaire, a measure of impairment on activities of daily living, were filled out by the parent.

Prior to the arrival of the participant for the second session, the NIRS was calibrated according to manufacturer's instructions. Upon arrival, the Edinburgh Handedness Questionnaire-Revised was verbally administered. Children were asked to perform ten tasks and hand use was recorded. (Note that one item (lighting a match) was substituted with threading a needle).

The NIRS sensors were placed symmetrically and horizontally on the child's forehead in the Fp1/F3 and Fp2/F4 positions of the International 10-20 system, in a manner similar to Weber et al. (2005). The placement of the sensors in line with the gyrus frontalis superior and middle gyrus frontalis (Homan, Herman, & Purdy, 1987), which is a portion of the dorsolateral prefrontal cortex. The head was measured with a tape measure from the nasion to the inion. To secure the sensors to the forehead and to prevent ambient light from being detected by the sensor, elastic tape was wrapped around the sensors and head, and the elastic tape was then covered by a thick black headband. After verifying that the all 16 emitters were not pinched or obstructed and that the sensors were completely covered and secured to the head, the overhead lights were dimmed.

Data collection commenced with the acquisition of a baseline measurement. Children sat quietly in a chair in front of a blank computer screen for 45 seconds. They were not asked to do

anything or spoken to during this time. After the baseline, a computerized version of the Stroop and WCST and reaction time tasks were performed while brain activity was monitored with NIRS. Session one required 60 to 90 minutes to complete testing and session two required 60 minutes.

After completion of the computer tasks, the children completed the single reaction time task followed by GNG and GNG-DT. The SRT was explained and participants were given at least ten practice trials to become familiar with the task. Without break, participants completed 16 trials of the SRT. Following instructions for the GNG, participants completed 28 trials. The same pattern was followed for GNG-DT.

Data Reduction and Analysis

Behavioral variables. For the Stroop task, separate means were calculated for congruent and incongruent trials for correct responses (percentage of the total correct) and reaction time (ms). There were reaction time values at or above three SDs from the mean, so they were removed (5% in DCD group and 6% in TD) and the mean imputed. For the WCST, the t score for perseverative errors were reported. Reaction times for the GNG tasks were logarithmically transformed due to skewness. A separate reaction time mean was then calculated for all three reaction time tasks (ms).

NIRS. Mean values of oxygenated hemoglobin and deoxygenated hemoglobin were measured and expressed as a percentage of oxygenation (oxygenated hemoglobin/ total hemoglobin). For the Stroop task, the mean for the 45 second baseline period was subtracted from the mean for the time during which it took each child to complete the task (approximately 100 seconds). For the WCST, the mean for the 45 second baseline was subtracted from the mean of the first 25 seconds of the WCST, a protocol similar to Moriguchi and Hiraki (2009). This interval was selected because cognitive activity is more similar between participants early in the task. For all three reaction time tasks, the mean for the 45 second baseline period was subtracted from the mean

for the time during which it took each child to complete each reaction time task: GNG, GNG-DT, and SRT.

Analyses were conducted using SAS (version 9.2). Because of unequal distribution of mean values, nonparametric analyses were used. The Kruskal-Wallis Test was used to compare group means for correct responses and reaction time in Stroop, perseverative errors in WCST, reaction time and movement time.in the GNG and GNG-DT. Errors in GNG and GNG-DT were tested using chi-square. Percent oxygenation for the left and right hemisphere was examined within each group for each task using the Wilcoxon Signed Ranks test.

Effect sizes were calculated to assess the meaning of differences (0.8 or greater considered large, 0.5 moderate and 0.2 small; Thomas, Salazar, & Landers, 1991). Because small sample sizes can inflate effect sizes (Hedges, 1981), a large effect was interpreted at 1.0 and small effect at 0.5 or below. The Phi coefficient value was used for effect size for the chi-square analysis with a small effect being 0.1, medium 0.3 and large 0.5 (Cohen, 1988).

We used a two-tailed statistical test for correct responses (Stroop), perseverative errors (WCST), and errors (GNG and GNG-DT), and a one-tailed test for reaction time, movement time, and percent oxygenation because we expected children with DCD to exhibit longer times and less rightward activation. Alpha was set at 0.05.

RESULTS

Means and standard deviations for all behavioral variables are presented in Table 2. Results for the behavioral data will be presented first followed by the NIRS data. Activation for the left and right hemispheres for baseline and for each task per participant is presented in Figure 2.

Table 2. Performance scores on Wisconsin Card Sort Task (WCST) and Stroop task for each group. Standard deviations are presented in parentheses and the range of scores in brackets.

Group	**DCD**	**TD**
WCST		
Perseverative Errors	10.1 (6.49) [5-22]	11 (5.35) [6-25]
Stroop		
Accuracy		
Congruent	1(0) [1]	0.984 (0.125) [0-1]
Incongruent	0.935 (0.247) [0-1]	0.927 (0.261) [0-1]
Reaction Time	1212 (528.7)	1069 (290.7)
Congruent	[568-3136]	[558-2472]
Incongruent	1311 (489.0) [605-2839]	1118.1 (290.6) [487-2826]

Behavioral

Stroop. The Kruskal-Wallis Test revealed no differences between groups for either condition for correct responses. The DCD group's reaction time was slower compared to TD, X^2 (1, n=14) = 34.3, $p < 0.0001$, d = 0.20.

WCST. The Kruskal-Wallis Test revealed no differences between groups on perseverative errors.

Go/Nogo and Go/Nogo-DT. Reaction time for DCD group was longer compared to TD, but the Kruskal-Wallis Test did not reveal statistical differences between groups in the GNG or GNG-DT. Children with DCD did exhibit a slower movement time in the GNG task, X^2 (1, n=14) = 3.92, $p = 0.048$, d = 2.1, and in GNG-DT, X^2 (1, n=14) = 8.27, $p = 0.004$, d= 4.42. The number

of errors during the GNG differed between groups, c^2 (1, 391) = 5.50, p = 0.019, d = 0.56, but the number of errors did not differ between groups in GNG-DT.

SRT. As above, the DCD group RT was longer compared to TD, but there were no statistical differences between groups. However, movement time was longer, X^2 (1, n=14) = 5.59, p = 0.018, d= 2.98.

NIRS

Stroop. The Wilcoxon Signed Rank Test revealed a trend for greater right hemisphere activation in the right hemispheres in the TD group, z = 1.47, p = 0.071, d = 0.79, but no difference in the DCD group.

WCST. Differences were not detected in the TD or DCD groups although the pattern was toward greater rightward lateralization in the TD group. .

GNG/GNG-DT. There was a trend for greater activation of the right hemisphere during the GNG task in the TD group, z = 1.53, p = 0.062, d = 0.82, but no differences were detected in the DCD group. No differences were found in percent oxygenation between the right and left hemispheres during the GNG-DT in the TD or DCD group.

SRT. Differences were found in percent oxygenation between the right and left hemispheres during the SRT in the TD group, z = 2.17, p = 0.015, d = 1.16 with greater activation in the right hemisphere, with no differences detected in the DCD group.

Figure 1. A) Percent change in oxygenation from baseline during Stroop. B) Percent change in oxygenation from baseline during Wisconsin Card Sort Task. C) Percent change in oxygenation from baseline during Simple Reaction Time Task. D) Percent change in oxygenation from baseline during Go/Nogo task. E) Percent change in oxygenation from baseline during Go/Nogo task. F) Percent change in oxygenation during Baseline.

Figure 1

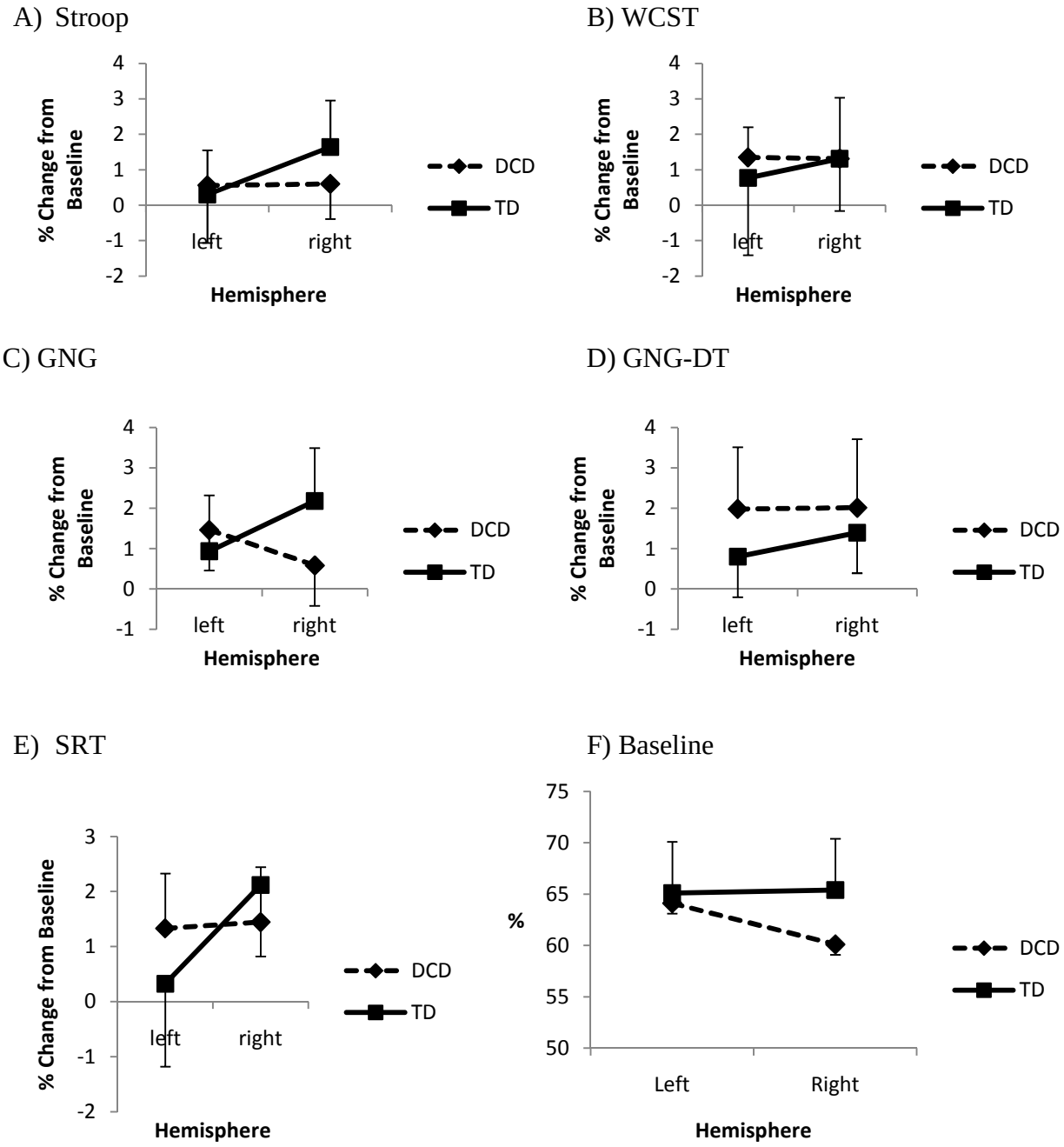
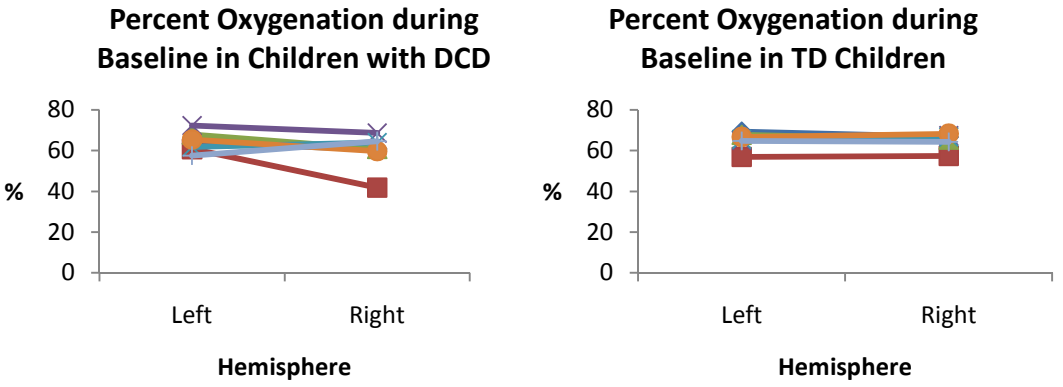
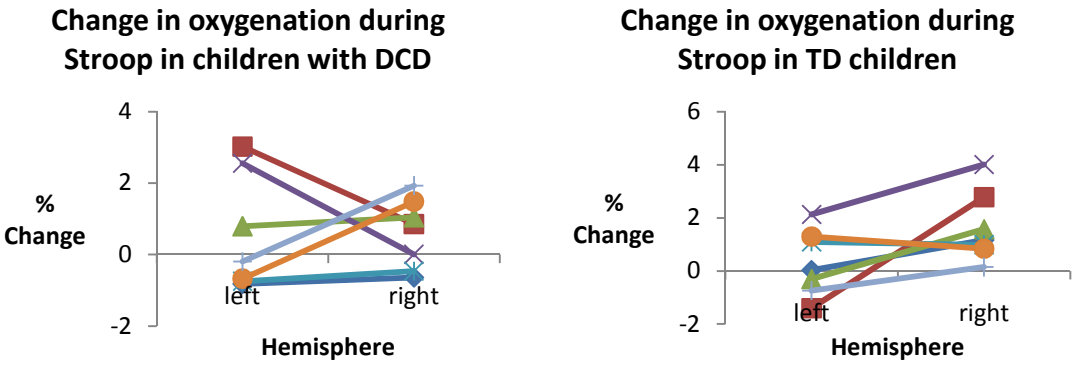


Figure 2. A) Percent oxygenation during Stroop for individual participants. B) Percent oxygenation during Wisconsin Card Sort for individual participants. C) Percent oxygenation during Simple Reaction Time task for individual participants. D) Percent oxygenation during Go/Nogo task for individual participants. E) Percent oxygenation during Go/Nogo-DT for individual participants.

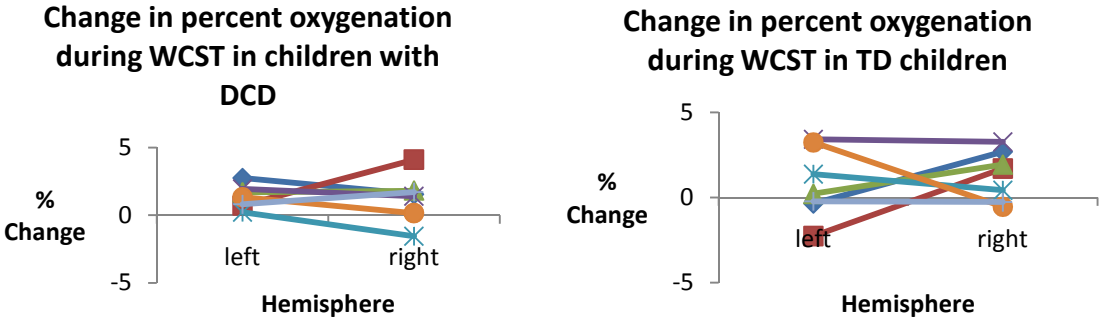
A) Baseline



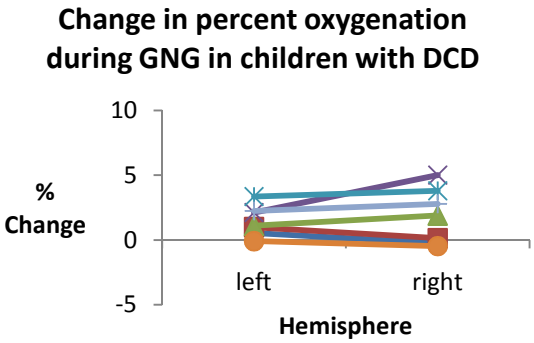
B) Stroop

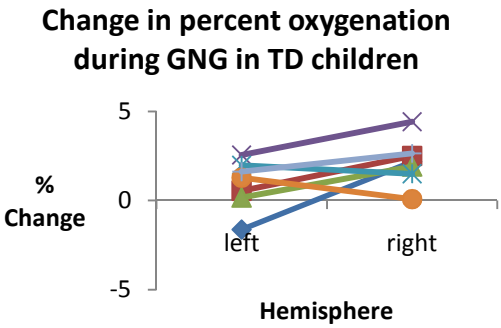


C) WCST

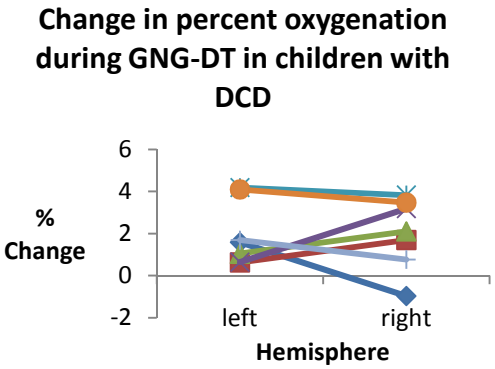


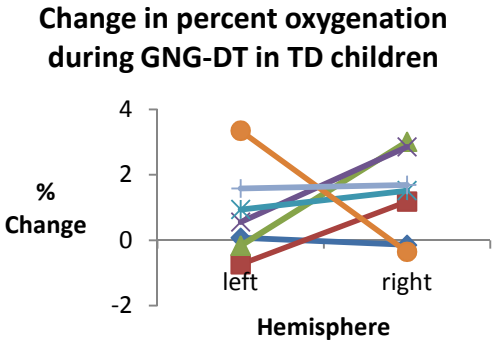
D) GNG



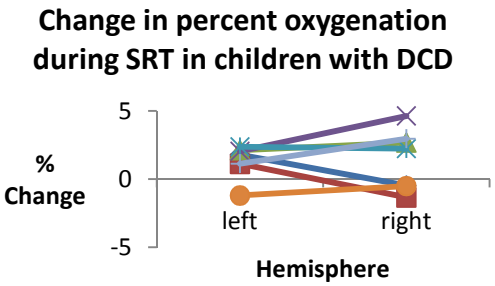


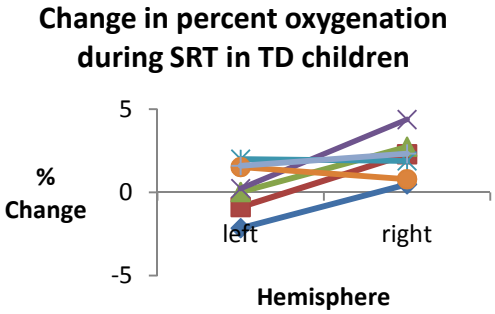
E) GNG-DT





F) SRT





DISCUSSION

The purpose of this study was to examine the relationship between executive processing in children with DCD and the corresponding brain activation. We hypothesized that children with

DCD would behaviorally perform the tasks in a manner similar to TD, in the Stroop, WCST and the GNG task, but not the GNG-DT. It was also hypothesized that the underlying brain activation would be different in all tasks. More specifically, we hypothesized that the TD children would activate the right hemisphere to a greater degree than the left hemisphere, whereas the children with DCD would not show this rightward lateralization.

Generally, the TD and DCD groups performed similarly on behavioral measures, but the TD group exhibited greater right-hemisphere activation. More specifically, the DCD group exhibited more errors only in GNG and a longer RT only in Stroop, but consistently exhibited longer movement times across tasks. Greater right hemisphere activation was observed in the TD group across tasks, with significance in SRT and a trend in Stroop and GNG. The DCD group exhibited similar activation between the two hemispheres for all tasks.

A lack of lateralization suggests that the children with DCD use different neural networks to accomplish the tasks. Although EF has often been used synonymously with prefrontal lobe function, research indicates damage to the prefrontal area will frequently, but not always, result in impaired EF (Baddeley, Della, Papagno, & Spinnler, 1997). Subcortical (Heyder, Suchan, & Daum, 2004) and cerebellar lesions (Bellebaum & Daum, 2007) have been shown to result in similar impairments. Further, decreased frontostriatal activation using fractional anistropy (a measure of diffuser tensor imaging) was implicated in impaired EF during a GNG task in children and adults with ADHD (Casey et al., 2007). Taken together, the research indicates that multiple structures are involved in EF, and damage to a single area will not necessarily result in impairment.

Children with DCD appear to be using different circuits for EF. Other researchers have found similar results and described similar interpretations. Querne et al. (2008) using fMRI to test

children with DCD found greater activation in networks connecting the parietal lobe to the anterior cingulate and parietal to the middle frontal cortex while performing a GNG task. When performing a trail-tracing task Zwicker and colleagues (2010) found greater fMRI activation in the anterior cingulate in children with DCD compared to TD and underactivation in the cerebellar networks (Zwicker et al., 2011).

Interestingly, brain lateralization in the TD group was strongest in simple reaction time. This task involves minimal executive processing while emphasizing speed of processing. Thus, the common denominator for differences in lateralization between the groups appears to be speed of processing, not executive processing. Notwithstanding, null results are difficult to assert given that the study is underpowered and had a very small sample size.

A second finding was that the DCD group generally exhibited a longer reaction time across tasks (though non-significant), with the difference reaching statistical significance for the Stroop. In addition, movement time was longer in simple reaction time and in the GNG task. This longer reaction time is consistent with many other studies in which these children exhibit slower information processing (such as Hyde & Wilson, 2010 and Mandich et al., 2002). Interestingly, the cerebellum has been shown to mediate information processing through cortico-cerebellar loops (Heydar et al., 2004). The cerebellum has also been implicated in higher cognitive processing (Krienen & Buckner, 2009), such as memory (Ben-Yehudah et al., 2007; Gottwald et al., 2004), and attention (Bellebaum & Daum, 2007). More specifically, Glickstein and Doron (2008) found separate circuits originating in the motor and pre-motor areas, and prefrontal cortex projecting to the pons, then cerebellum (motor projections traveling to the dorsal aspect of the dentate nucleus, while the prefrontal projections traveling to the ventral part of the dentate nucleus), then back to

the cortex via the thalamus. Thus, our reaction time findings together with the results from NIRS may further implicate these cerebellar circuits.

There were several limitations in this study. One limitation is the small number of children in each group, thus making the sample less representative and decreased statistical power. We conducted an *a posteriori* power analysis and found power to be 0.18. A second limitation is that we had only prefrontal sensors so we could not examine changes in other areas of the cortex. Moreover, the NIRS sensors sample only a small area of the dorsolateral prefrontal cortex (DLPFC). Areas outside of the DLPFC may be activated more intensely by some of the tasks used in this study.

The current study makes a unique contribution to what is known about DCD. Near infrared spectroscopy confirms that children with DCD utilize alternative brain circuitry to accomplish cognitive tasks despite similar behavioral performance. Further, three different tasks that utilize inhibitory networks were used, and revealed three different sets of results from which we can suggest 1) different inhibitory tasks exploit different networks or brain areas, 2) children with DCD do not fail to inhibit correctly in all tasks, perhaps due to complexity, and 3) children with DCD do not demonstrate slowed reaction time in all EF tasks. Moreover, we are the first to use NIRS to assess brain activation in children with DCD. The use of NIRS is advantageous because it provides high temporal resolution as well as a way to measure a greater variety of tasks in a testing environment that is less constrained than other neuroimaging techniques, such as functional magnetic resonance imaging, positron emission tomography and electroencephalography.

Future directions for this line of research involve the application of NIRS during a blocked Stroop task, such that percent oxygenation during congruent and incongruent blocks can be measured. Similarly, the hemodynamic response to perseverations during the WCST may

illuminate more specific changes during that task and allow inferences to be made regarding the role of the DLPFC in error processing.

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